REMARKS

Reconsideration of the rejections set forth in the Office action mailed February 8, 2005 is respectfully requested. Claims 13-17, 21, and 24-29 are currently under consideration. No amendments are made with this response.

I. Rejections under 35 U.S.C. §103(a)

Claims 13-17, 21, and 24-29 were rejected under 35 U.S.C. §103(a) as being unpatentable over Murphy *et al.*, *Proc. Natl. Acad. Sci. USA* **95**:1517, 1998, in view of Liotta *et al.*, U.S. Patent No. 6,153,596. This rejection is respectfully traversed for the following reasons.

A. The Invention

The applicant's invention, as embodied in independent claim 13, is directed to a method of identifying peptoids, in a library of different-sequence peptoids, which are effective in transfecting a cell with an oligonucleotide. The method comprises the steps of (i) contacting each different-sequence peptoid in the library with an oligonucleotide, to form a plurality of peptoid-oligonucleotide mixtures; (ii) contacting each said mixture with a cell; (iii) screening each cell for transfection of the oligonucleotide, to identify transfected cells; and (iv) identifying transfecting peptoids in mixtures contacted with transfected cells.

B. The Cited Art

Murphy *et al.*, as discussed in a previous response, describes the identification of cationic peptoids which are effective in the delivery of plasmid DNA. The DNA species employed for screening is pCMV-km-LUC (see "Plasmids and Cell Lines" on page 1518), which is known to have over 4,000 basepairs (as reported, for example, in U.S. Patent No. 6,468,986). As noted by the Examiner in the current Office Action, this reference does not address transfection of oligonucleotides by peptoids.

Liotta *et al.* describes the use of polycationic polymers, which may include peptoids (e.g., Fig. 2; col 14, lines 40-57; col 15, lines 31-40; col 16, lines 1-11), for transfection of nucleic acids, including oligonucleotides (e.g., Abstract; col 6, lines 12-14).

Liotta *et al.* teaches that sequence per se is not an important factor in electrostatic binding between nucleic acids and cationic peptides or peptoids. Rather, Liotta *et al.* teaches that, in cationic oligomers, such as peptoids, length of oligomer and spacing of cationic side groups are critical factors in determining their effectiveness in oligonucleotide transfection. The reference emphasizes the use of a "size-selected polycationic oligomer which neutralizes the negative charge of the nucleic acid" (e.g., col 7, lines 56-57) and also emphasizes the spacing of cationic groups in the oligomer: "Cationic side groups are spaced in the cationic oligomer to substantially match the spacing between negatively charged groups in the nucleic acid backbone" (col 8, lines 4-6). See also col 10, lines 27-30; col 18, lines 18-21 and 58-67; col 19, lines 38-42 and 57-62; etc. The reference further teaches that the appropriate spacing of cationic side groups is that in which cationic side chains are on "alternating repeating units along the oligomer chain" (col 8, lines 42-45), as illustrated in Figures 1-2.

With respect to different types of side chains that may be used, Liotta *et al.* teaches that appropriate cationic side chains in peptoids are side chains of amino acids, such as lysine or arginine (e.g. col 15, lines 33-34), and that appropriate neutral side chains, which alternate with the cationic side chains, are lower alkyl groups (e.g. col 15, lines 45-46 and col 16, lines 1-5). Little emphasis is placed on the nature of these groups other than their being charged or neutral.

The data presented in the patent supports these conclusions. For example, in Example 8, Liotta *et al.* test a series of cationic oligomers having the same sequence; i.e., repeating units of Lys-Ala, in a gel mobility shift assay. The only difference between the oligomers tested is their length, i.e. the number of repeating units (12, 24, or 28) (see column 36, lines 41-42). The reference emphasizes that the length of the oligomer had a significant effect on the mobility of a 28-base oligonucleotide in the gel shift assay (Example 8, column 37, lines 1-10). Similarly, the longer oligomer, having the same number of repeating units as bases in the oligonucleotide, was much more efficient in transfecting the oligonucleotide into cells (Example 9, col 38, lines 20-30).

Liotta *et al.*, therefore, teaches that length of oligomer and spacing of cationic side groups, not sequence per se, are the primary factors in determining the effectiveness of cationic oligomers in oligonucleotide transfection. Its teachings would direct the skilled

person desiring to deliver an oligonucleotide to a cell to employ a cationic peptide or peptoid which (1) is similar in length to the oligonucleotide to be delivered, (2) has the same number as charges as the oligonucleotide, and (3) has cationic side groups alternating with neutral side groups, to give an appropriate spacing of positively charged side groups. There is no suggestion in Liotta *et al.* that varying the nature or sequence of these groups from this general pattern (i.e., varying the sequence of the peptoids) would be desirable or would increase transfection efficiency.

There is no motivation provided in Liotta, therefore, to screen a "library of different-sequence peptoids" for oligonucleotide transfection, as claimed by the applicants.

As noted above, Murphy *et al.* do not address transfection of oligonucleotides at all. Therefore, neither reference, taken alone or in combination, suggests the process claimed by the applicants.

In view of the foregoing, the applicant respectfully requests the Examiner to withdraw the rejection under 35 U.S.C. §103(a).

II. Conclusion

In view of the foregoing, the applicant submits that the claims now pending are now in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

Respectfully submitted,

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